

**WHAT IS CLAIMED IS:**

1. A surface-modified lipoprotein-like oil-in-water emulsion having a lipophilic core surrounded by a monolayer of amphiphilic or polar lipids, in a non-ionic aqueous phase, the emulsion having a mean particle diameter of the oil phase of between 50 to 150 nm with at least 98% of the particles being between 50 to 250 nm, the lipophilic core containing at least one lipophilic agent or lipophilic derivative of a water-soluble agent which is diagnostically or therapeutically active or inactive, and the monolayer components including an emulsifier, a derivatized polyethylene glycol or polyethylene glycol-linked lipid, and a sterol.
2. The oil-in-water emulsion of claim 1 wherein the lipophilic core comprises up to 50% (w/v) of the total emulsion composition.
3. The oil-in-water emulsion of claim 2 wherein the lipophilic core comprises between about 10% and 40% (w/v) of the total emulsion composition.
4. The oil-in-water emulsion of claim 1 wherein the at least one lipophilic or lipophilic derivative of a water-soluble agent is a pharmaceutically acceptable nonpolar lipid.
5. The oil-in-water emulsion of claim 4 wherein the pharmaceutically acceptable nonpolar lipid is a triglyceride.
6. The oil-in-water emulsion of claim 5 wherein the triglyceride is a biocompatible oil of animal or vegetable origin.
7. The oil-in-water emulsion of claim 5 wherein the triglyceride is a synthetic or semi-synthetic lipid.
8. The oil-in-water emulsion of claim 7 wherein the synthetic or semi-synthetic lipid is triolein.
9. The oil-in-water emulsion of claim 7 wherein the triglyceride is an halogenated triglyceride.
10. The oil-in-water emulsion of claim 1 wherein the lipophilic core comprises at least one pharmacologically inert nonpolar lipid and a contrast agent which is lipophilic or a lipophilic derivative of a water-soluble contrast agent.

11. The oil-in-water emulsion of claim 10 wherein the lipophilic core comprises at least one pharmacologically acceptable inert nonpolar lipid and a contrast agent which is a halogenated triglyceride.

5 12. The oil-in-water emulsion of claim 10 wherein the ratio of pharmacologically inert nonpolar lipid to contrast agent ranges from about 0.1:1.0 to 2:1 on a weight to weight basis.

13. The oil-in-water emulsion of claim 12 wherein the ratio of pharmacologically inert nonpolar lipid to contrast agent is 1:1 on a weight to weight basis.

10 14. The oil-in-water emulsion of claim 1 wherein up to 10% (w/v) of the emulsion is an amphipathic or polar lipid.

15 15. The oil-in-water emulsion of claim 14 wherein the amphipathic or polar lipid is an emulsifier.

16. The oil-in-water emulsion of claim 14 wherein the emulsifier is a natural, synthetic, or semi-synthetic phospholipid.

15 17. The oil-in-water emulsion of claim 16 wherein the phospholipid is synthetic or semi-synthetic.

18. The oil-in-water emulsion of claim 17 wherein the phospholipid is dioleoylphosphatidylcholine.

20 19. The oil-in-water emulsion of claim 1 wherein up to 5% (w/v) of the emulsion is a sterol.

20. The oil-in-water emulsion of claim 19 wherein the sterol is cholesterol.

21. The oil-in-water emulsion of claim 19 wherein between about 0.4 to 0.5% (w/v) of the emulsion is a sterol.

25 22. The oil-in-water emulsion of claim 21 wherein the molar ratio of cholesterol to emulsifier is between 0.05 to 0.70.

23. The oil-in-water emulsion of claim 1 wherein the emulsion further includes a up to 5% (w/v) of an osmolality adjusting agent.

24. The oil-in-water emulsion of claim 23 wherein the osmolality adjusting agent is anhydrous glycerol.

25. The oil-in-water emulsion of claim 1 further comprising a sufficient amount of an antioxidant to prevent oxidation of the emulsion.

5 26. The oil-in-water emulsion of claim 25 wherein the antioxidant is  $\alpha$ -tocopherol.

26. The oil-in-water emulsion of claim 1 wherein the emulsion comprises up to about 5% (w/v) derivatized polyethylene glycol or polyethylene glycol-linked lipid.

10 27. The oil-in-water emulsion of claim 26 wherein the derivatized polyethylene glycol or polyethylene glycol-linked lipid comprises between about 0.1 and 30 mole percent of the monolayer components.

28. The oil-in-water emulsion of claim 26 wherein the derivatized polyethylene glycol or polyethylene glycol-linked lipid is selected from the group consisting of MPEG-linked phosphatidylethanolamine, MPEG-2000-1,2-distearoyl and  
15 MPEG-2000-1,2-dioleoyl phosphatidylethanolamine.

29. The oil-in-water emulsion of claim 26 wherein the derivatized polyethylene glycol or polyethylene glycol-linked lipid is methoxy polyethylene glycol having a molecular weight between about 1000 and 6000.

20 30. An oil-in-water emulsion comprising:

- a) up to 50% (w/v) lipophilic core which is a pharmaceutically inert fat or oil of natural, synthetic, or semi-synthetic origin and a lipophilic contrast agent or radiopharmaceutical or lipophilic derivative of a water-soluble contrast agent or radiopharmaceutical;
- 25 b) up to 10% (w/v) phospholipid emulsifier;
- c) up to about 5% (w/v) cholesterol;
- d) up to 5% derivitized polyethylene glycol or polyethylene glycol-derivative of a phospholipid (w/v);
- d) up to 5% (w/v) of osmolality adjusting agent;

- e) optionally, up to 1 % antioxidant;
- f) the remainder being water, suitable for parenteral administration.

31. The oil-in-water emulsion of claim 30 wherein the lipophilic contrast agent or radiopharmaceutical or lipophilic derivative of a water-soluble contrast agent or radiopharmaceutical is a polyhalogenated triglyceride.

32. The oil-in-water emulsion of claim 30 wherein the lipophilic contrast agent or radiopharmaceutical or lipophilic derivative of a water-soluble contrast agent or radiopharmaceutical is an aliphatic ester of a water-soluble contrast agent.

33. The oil-in-water emulsion of claim 32 wherein the aliphatic ester of a water-soluble contrast agent is selected from the group consisting of aliphatic esters of iopanoic, diatrizoic, and acetrizoic acid.

34. The oil-in-water emulsion of claim 33 wherein the aliphatic ester is selected from the group consisting of ethyl iopanoate and butyl iopanoate.

35. An oil-in-water emulsion comprising:

- a) between 10% and 50% (w/v) of a pharmacologically inert triglyceride and a polyhalogenated triglyceride wherein the molar ratio of pharmacologically inert triglyceride to polyhalogenated triglyceride is in the range of 0.1:1 and 2:1 (w/w);
- b) up to about 9.9 % (w/v) phospholipid comprising dioleoylphosphatidylcholine and MPEG-linked phospholipid;
- c) up to 4.8 % (w/v) cholesterol, wherein the molar ratio of cholesterol to total phospholipid is in the range of 0.05 to 0.70;
- d) 5% (w/v) glycerol;
- e) 0.1-0.6 %  $\alpha$ -tocopherol; and
- f) the remainder of the emulsion being water, the emulsion having a mean particle diameter of the oil phase between 50 to 150 nm with at least 98% of the particles being between 50 to 250 nm.

36. The oil-in-water emulsion of claim 35 wherein the molar ratio of pharmacologically inert triglyceride and polyhalogenated triglyceride is 1:1.

37. The oil-in-water emulsion of claim 35 wherein the amount of cholesterol is in the range of 0.4 to 0.5 % (w/v).

38. The oil-in-water emulsion of claim 37 wherein the molar ratio of cholesterol to total phospholipid is 0.4.

5        39. The oil-in-water emulsion of claim 35 wherein the polyhalogenated triglyceride is a lipophilic diagnostic agent selected from the group consisting of iodinated arylaliphatic triglyceride analogs having a 1,3-disubstituted triglyceride backbone with a 3-substituted 2,4,6-triiodophenyl aliphatic chain or a moniodophenyl aliphatic chain.

10       40. The oil-in-water emulsion of claim 39 wherein the polyhalogenated triglyceride is 2-oleoylglycerol-1,3-bis[7-(3-amino-2,4,6-triiodophenyl)heptanoate].

41. The oil-in-water emulsion of claim 39 wherein the polyhalogenated triglyceride is 2-oleoylglycerol-1,3-bis[4-(3-amino-2,4,6-triiodophenyl)butanoate].

42. The heat stable hepatocyte-selective oil-in-water emulsion of claim 31  
15 wherein the polyhalogenated triglyceride is a 1,2,3-trisubstituted triglyceride backbone with a 3-substituted 2,4,6-triiodophenyl saturated or unsaturated aliphatic chain or a moniodophenyl aliphatic chain.

43. The oil-in-water emulsion of claim 35 wherein the polyhalogenated triglyceride is a fluorinated triglyceride.

20       44. A method of computerized tomographic imaging comprising the steps of:

a) administering an imaging amount of the oil-in-water emulsion of claim 35 to a mammal wherein the oil-in-water emulsion contains a computerized tomography imaging agent; and

25       b) when the imaging amount of the oil-in-water emulsion has reached the site to be imaged, carrying out computerized tomographic imaging of the site.

45. A method of treating a living being in need of treatment comprising the step of administering an effective amount of the oil-in-water emulsion of claim 1

which contains a therapeutically active lipophilic agent or a lipophilic derivative of a water-soluble agent.

46. A method of computerized tomographic imaging comprising the steps of:

- 5           a) administering an imaging amount of the oil-in-water emulsion of claim 35 to a mammal wherein the oil-in-water emulsion contains a computerized tomography imaging agent; and
- b) when the imaging amount of the oil-in-water emulsion has reached the site to be imaged, carrying out computerized tomographic imaging of the site.

10          47. A method of making a blood pool selective oil-in-water emulsion comprising the steps of:

- (a) preblending the lipophilic components of an oil-in-water emulsion including nonpolar lipids, polar lipid emulsifiers, and other lipophilic components to form a premixed lipid phase;
- 15          (b) homogenizing the premixed lipid phase and aqueous components to form a crude oil-in-water emulsion; and
- (c) subjecting the crude oil-in-water emulsion to ultra high energy mixing to produce a fine oil-in-water emulsion having a mean particle diameter of the oil phase between 50 to 150 nm with greater than 98% of the particles being less than 250
- 20 nm.

48. The method of claim 47 comprising the further step of:  
subjecting the fine oil-in-water emulsion to sequential filtering.